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EXAMINER	
DECLOUX, AMY M	
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/081,281	Applicant(s) KINDSVOGEL ET AL.	
	Examiner Amy M. DeCloux	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2003 and 23 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-49* is/are pending in the application.

4a) Of the above claim(s) *27-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,3* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Notice to comply with Requirements for Sequence Disclosures.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 39-49 in Paper No. 9 filed 9-23-02, is acknowledged. The traversal is on the ground(s) that since Groups I and II stem from a common concept and theory, it would not place substantially greater burden on the examiner to prosecute the claims of both Groups I and II.

This is not found persuasive because a search of methods comprising each of the recited species are distinct for the reasons given in the restriction mailed 3-26-02 (Paper No. 5), and as such have acquired a separate status in the art because of their recognized divergent subject matter. MPEP 803 states that: "For the purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation, either separate classification, separate status in the art, or different field of search. Because a search in the non-patent literature of the heterodimer encompassed by Group I would not be co-extensive with a search of an expression cassette encompassed by Group II, an examination and search of a both groups in a single application would constitute a serious undue burden on the Examiner, and therefore, restriction for examination purposes as indicated is proper.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's election of SEQ ID NO:33 in Paper No. 12, filed 2-20-02 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the species election has been treated as an election without traverse (MPEP § 818.03(a)). Because art was found on the elected species, the search was not extended to any other species. Claims that read on the elected species are Claims 39-49.

Claims 27-38 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 39-49 are being considered presently.

Specification

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2).

However, this application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Sequences are disclosed in the specification and in the claims that require a SEQ ID NO: Tag, (for example see claims 43 and 44 which recite the sequence GASAG which corresponds to SEQ ID NO:29, and the sequence GGSGGS which corresponds to SEQ ID NO: 30 or 31, and non-tagged sequences disclosed on page 49, line 16, and page 56, line 8, and Tables 3 and 4). Applicants are required to resubmit a substitute disk and paper copy of the sequences according to the attached "Notice to Comply with the Sequence Rules." Applicant is reminded of the sequence rules which require a submission for all sequences of more than 9 nucleotides or 3 amino acids (see 37 C.F.R. 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 and 44 are indefinite in their recitation of GGSGGS, because it is not clear if said sequence refers to SEQ ID NO:31 which is GGGSGGS or to SEQ ID NO:30 which is GGSGG.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international

application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39 and 47 are rejected under 35 U.S.C. § 102(e) and under 35 U.S.C. § 102(b) as being anticipated by Clark et al (U.S. Patent No. 5, 284,935, filed Dec. 28, 1990, issued Feb 8, 1994).

'935 teaches an expression cassette encoding a recombinant complex of MHC wherein the α1 and β1 domains of class II MHC are linked through a flexible linker (see entire patent, especially Figure 4 and column 8, lines 10-17). '935 also teaches that a peptide epitope may be connected to the N terminal end using recombinant techniques (see entire patent, especially the last paragraph of column 14 and the first two paragraphs of column 15), and will effect CD4+ helper T cell mediated immune response (see entire patent including column 13, lines 47-58). Therefore, the referenced teachings anticipate the claimed invention.

It is noted that the phrase "consisting essentially of" recited in the instant claims is considered open language. MPEP 2111.03 states that for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963).

Claims 39, 41-42 and 46-47 are rejected under 35 U.S.C. § 102(e) as being anticipated by Mottez et al ((IDS) U.S. Patent No. 5,976,551, filed June 7, 1995, issued Nov. 2, 1999, and which has priority back to Nov. 1991), as evidenced by Madsen et al. (Nat. Genetics (1999) 23(3):343-7, ABSTRACT ONLY).

Mottez et al teaches an expression cassette encoding an MHC class II complex heterodimer which comprises a β1 domain linked by a peptide spacer to an α1 domain that associates with an antigenic peptide (see entire patent, especially figure 4, column 5, lines 57-67 and column 6, lines 1-10) as recited in the instant claims. Mottez et al teaches linker segments or spacers between the MHC domains from 2 to 30 amino acids (see entire patent, especially column 8, lines 40-64), which encompass the 5-25 amino acids recited in claim 47. Mottez et al also teaches signal sequences which can be used in the cassettes (see entire patent, especially column 31 and columns 39-42) as recited in claim 46. Mottez et al also teaches that MHC Class II associated with peptide antigen stimulates T helper cells (CD4) and lists peptides that can be associated with the product of said expression cassettes, (see entire patent, especially columns 1-2 and column 10 and Table 6). Mottez et al also teach that said expression cassette comprises a domain from the DR2 HLA class II loci (see entire patent, including column 7, Table 3,) which is synonymous with DRA*0101/DRB1*1501 recited in instant claims 41-42 (see the Abstract of Madsen et al.). The open language of the phrase "consisting essentially of" recited in the instant

claims is noted as discussed supra. Therefore, the referenced teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of *35 U.S.C. § 103* which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under *subsection (f) or (g)* of *section 102* of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39 and 41-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al (U.S. Patent No. 5, 284,935, filed Dec. 28, 1990, issued Feb 8, 1994) or Mottez et al ((IDS) U.S. Patent No. 5,976,551, filed June 7, 1995, issued Nov. 2, 1999, and which has priority back to Nov. 1991), in view of Strominger et al (U.S. Patent No. 5,874,531, filed March 7, 1995, issued Feb. 23, 1999), and in view of Fugger et al (PNAS 91:6151-6155, 1994).

Clark et al and Mottez et al teach as above. However, neither patent teaches specifically an expression cassette encoding a soluble fused MHC Class II heterodimer wherein the MHC class II chain is selected from at least one of human DRB*1501 beta chain and a human DRA*0101 alpha chain, as recited in claims 41 and 42.

Strominger et al teaches that the HLA DR1beta*1501 is a genetic marker for MS and that HLA DR1beta*1501 is reactive with the immunodominant autoimmune peptide MBP (84-102) and causes T cell expansion in vitro (see entire article, especially column 2, lines 4-19).

Fugger et al teach an MHC class II complex that comprises a human DRA*0101 alpha chain that binds an antigen associated with autoimmune disease, (see entire article, especially the Abstract).

Therefore, it would have been obvious to one of skill in the art at the time the invention was made who wanted to study autoimmune disease, to have made and used an expression cassette encoding a recombinant MHC Class II heterodimer that would form a peptide binding groove that associates with an antigenic peptide, by substituting the human DR1beta*1501 beta chain taught by Strominger et al and/or a human DRA*0101 alpha chain taught by Fugger et al, into the expression vector encoding the MHC Class II heterodimer taught by either Clarke et al or by Mottez et al, because Clarke et al teach heterodimers of MHC class II would be useful in treating autoimmune diseases.

Claims 39-40, 45 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al (U.S. Patent No. 5, 284,935, filed Dec. 28, 1990, issued Feb 8, 1994) or Mottez et al ((IDS) U.S. Patent No. 5,976,551, filed June 7, 1995, issued Nov. 2, 1999, and which has priority back to Nov. 1991), in view of Kappler et al. (U.S. Patent 5,820,866, filed 3-4-1994, issued 10-13-1998).

The '935 patent and the '551 patent teach as above.

However, neither the '935 patent nor the '551 patent teaches the claimed expression vector, which further comprises a third nucleic acid segment encoding a third polypeptide segment comprising an antigenic peptide that associates with the peptide binding groove of the MHC class II heterodimer, and a second linker segment encoding a second peptide linker and connecting in-frame the third and first nucleic acid segments. Also neither the '935 patent nor the '551 patent teaches the said second linker is about 5 to about 25 amino acids long.

Kappler et al. teaches a nucleic acid molecule having a sequence encoding peptide-linker MHC molecule comprising an antigenic peptide joined by a linker to an MHC segment, wherein said MHC Class II molecule contains the alpha 1 domain and the beta 1 domain, wherein said linker is from about 1 amino acid residue to about 40 amino acid residues, or from about 5 amino acid residues to about 30 amino acid residues (column 5, lines 23-60, column 9, lines 10-55, and the Abstract). Kappler teaches a linker is preferably between about 5 and about 30 amino acids long and no longer than 40 amino acids so that it does not inhibit binding between the antigenic peptide with an MHC protein or hinder interaction of an antigenic peptide with an MHC protein bound by peptide with a TCR (see entire patent, especially column 9, lines 39-55). Kappler et al teaches that a linker that stabilizes the association of an antigenic peptide with an MHC binding site, resulting in the formation of a stable composition that can be recognized by a TCR, and that said linker enhances the ability of a compound aggregate of antigenic peptide and MHC protein to act as a unit in triggering a desired immune response (see entire patent, including column 9, lines 1-15 and column 2, lines 13-28).

Therefore, it would have been obvious to one of skill in the art at the time the invention was made who wanted to regulate the immune response in a patient, to have made and used an expression cassette encoding a recombinant MHC Class II heterodimer such as one taught by Clarke or Mottez, and to have modified it so that it further comprises a third nucleic acid segment encoding a third polypeptide segment comprising an antigenic peptide that associates with the peptide binding groove of the MHC class II heterodimer, and a second linker segment encoding a second peptide linker and connecting in-frame the third and first nucleic acid segments, as taught by Kappler et al, because Kappler et al teaches that a peptide so linked to the MHC Class II molecule would stabilize the association of an antigenic peptide with an MHC binding site, resulting in the formation of a stable composition that can be recognized by a TCR, enhancing the ability of a compound aggregate of antigenic peptide and MHC protein to act as a unit in triggering a desired immune response, and because Clarke et al teaches that a recombinant MHC Class II heterodimer comprising an antigenic peptide will effect CD4+ helper T cell mediated immune response.

Further, one would have been motivated to have made and used said modification of the expression cassette taught by Kappler or Mottez, wherein said second peptide linker segment encodes a second peptide linker of about 5 to about 25 amino acids as taught by Kappler et al. because Kappler et al teaches that linker is preferably between about 5 and about 30 amino acids long and no longer than 40 amino acids, so that it does not inhibit binding between the antigenic peptide with an MHC protein or hinder interaction of an antigenic peptide with an MHC protein bound by peptide with a TCR.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 39, 40 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark et al (U.S. Patent No. 5, 284,935, filed Dec. 28, 1990, issued Feb 8, 1994) or Mottez et al ((IDS) U.S. Patent No. 5,976,551, filed June 7, 1995, issued Nov. 2, 1999, and which has priority back to Nov. 1991), in view of Kappler et al. (U.S. Patent 5,820,866, filed 3-4-1994, issued 10-13-1998) as applied to claims 39 and 40 above, and further in view of Strominger et al (U.S. Patent No. 5, 874,531, filed March 7, 1995, issued Feb. 23, 1999) .

Clark et al., Mottez et al., Kappler et al. and Strominger et al teach as above.

Neither Clark et al., Mottez et al., Kappler et al., nor Strominger et al., teaches the claimed expression vector, which further comprises a third nucleic acid segment encoding a third polypeptide segment comprising an antigenic peptide that associates with the peptide binding groove of the MHC class II heterodimer, and a second linker segment encoding a second peptide linker and connecting in-frame the third and first nucleic acid segments, wherein said third nucleic acid segment encodes a peptide consisting of SEQ ID NO:33.

Therefore, it would have been obvious to one of skill in the art at the time the invention was made who wanted to regulate the immune response in a patient, to have made and used an expression cassette encoding a recombinant MHC Class II heterodimer such as one taught by Clarke or Mottez, and to have modified it so that it further comprises a third nucleic acid segment encoding a third polypeptide segment comprising an antigenic peptide that associates with the peptide binding groove of the MHC class II heterodimer, and a second linker segment encoding a second peptide linker and connecting in-frame the third and first nucleic acid segments, as taught by Kappler et al, for the reasons discussed above, and to have made the third nucleic acid segment encoding a third polypeptide segment comprising an antigenic peptide to be the autoimmune antigenic peptide corresponding to residues 82-104 of myelin basic protein (SEQ ID NO:33, as recited in claim 49), since Strominger teaches that said peptide is reactive with MHC Class II molecules (specifically HLA DR1beta*1501) and causes T cell expansion and because Clarke et al teach heterodimers of MHC class II would be useful in treating autoimmune diseases.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy M. DeCloux whose telephone number is 703 306-5821. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 703 308-3973. The fax phone numbers for the organization where this application or proceeding is assigned are 703 872-9306 for regular communications and 703 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-0196.

Amy DeCloux, Ph.D.
Patent Examiner
Group 1640
April 6, 2003
Amy DeCloux 4-6-03